

State of the art in endocarditis treatment

Francesco Maria Bovenzi



Declaration of interest

I have nothing to declare!

Early clinical descriptions



French renaissance physician

Jean Fernel
(1497-1558)

**Earliest
report**

- Described unusual “outgrowths” from autopsy.
- Detected murmurs by placing hand on patient’s chest



Lazare Riviere
(1589-1655)

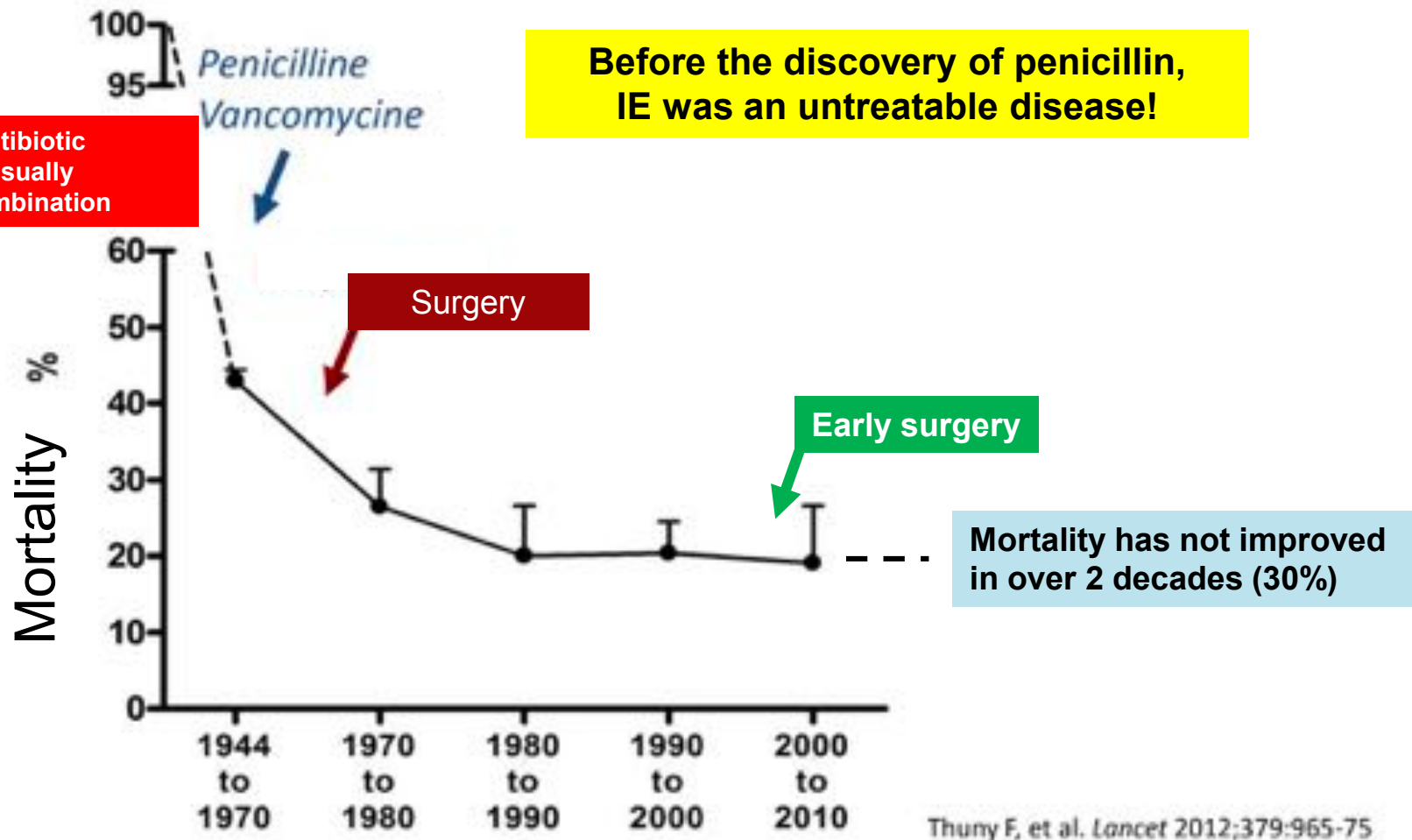


William Osler
(1849-1919)

**1881- Synthesized
work of others**



Evolution of the knowledge in the treatment from antibiotic therapy down to the early surgery!



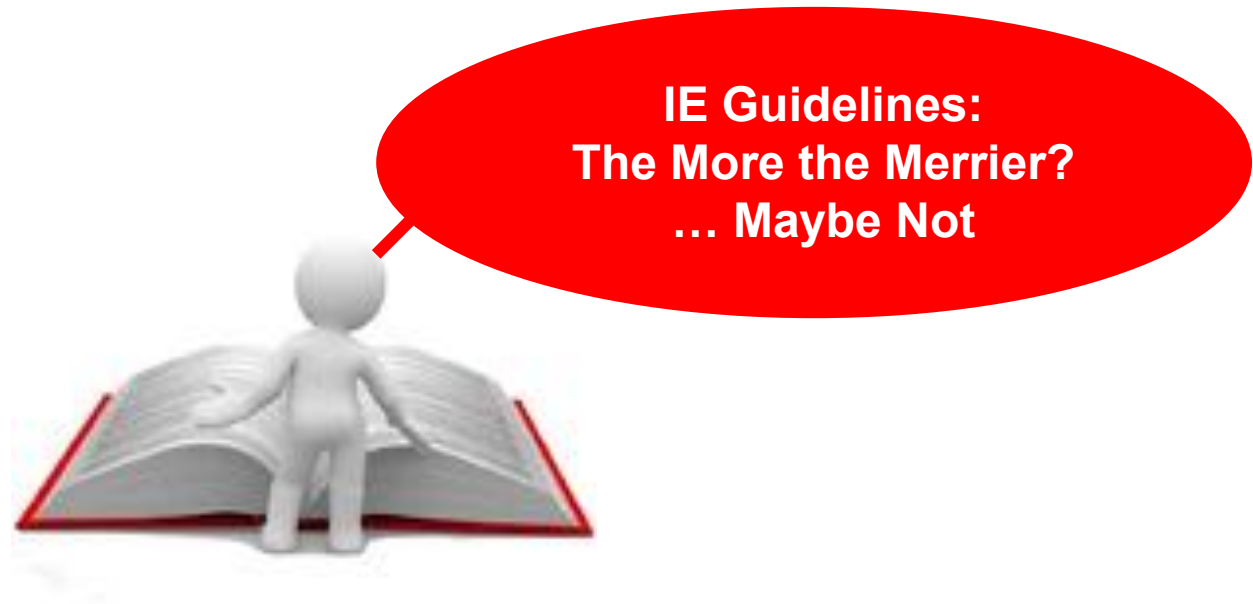
Challenges in Infective Endocarditis

Thomas J. Cahill, MBBS,^a Larry M. Baddour, MD,^b Gilbert Habib, MD,^{c,d} Bruno Hoen, MD, PhD,^e

Erwan Salaun, MD,^d Gosta B. Pettersson, MD, PhD,^f Hans Joachim Schäfers, MD,^g Bernard D. Prendergast, DM^h

- A **rare and devastating disease** with heterogeneous clinical manifestations
- Hospital **charges** \$120,000 per patient
- **Demographic changes**: in pre-antibiotic era it affected **young people**, now it affects **older and frailer** with comorbidities
- **Health care–acquired** in >25%.
- **S. aureus** (1/3 cases - ***The microbe makes the difference***: independent risk factor for in-H death!) overtook oral Streptococci
- **Antibiotic prophylaxis is a controversy**, today limited to high-risk groups
- **Only 7 RCT** due to: lack of funding, logistics problems and ethical debate
- Management is both a clinical and logistical challenge: **Team Work**
- The current priorities challenges are: **Stroke, CDREI, TAVI ...**
- **Surgery** is performed **in 50-60%** (higher in left-sided prosthetic valve), **but the right timing is uncertain.**
- **Guidelines don't help!**

**Guidelines are of great importance
since IE is specifically challenging
due to a marked disease heterogeneity**



**Over three cycles of Guidelines (2004 ➡ 2015 ESC and AHA)
the advice for IE has become
more extensive but less evidence-based
(the increase is only in LOE C recommendations)**

... To clarify the **change in recommendations over time** and to **detect gaps in knowledge**

Temporal Changes in Infective Endocarditis Guidelines during the last 12 years:

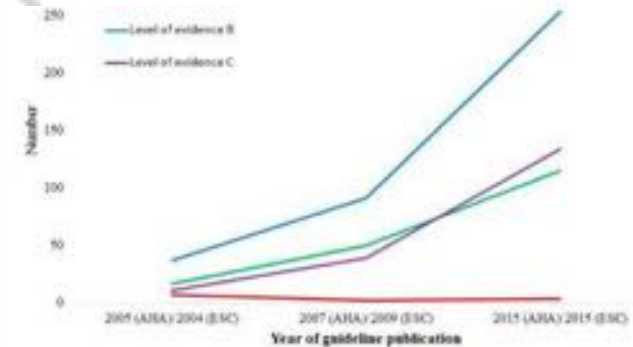
High-level Evidence Needed

Lauge Østergaard MB¹, Nana Valeur MD², Henning Bundgaard MD DMSc¹, Jawad H. Butt MB¹, Nikolaj

Ihlemann MD PhD¹, Lars Køber MD DMSc¹, Emil L. Fosbøl MD PhD¹

They categorized and combined IE guidelines published by AHA and ESC in three time periods:

- 1) 2004 (AHA) and 2005 (ESC)
- 2) 2007 (AHA) and 2009 (ESC)
- 3) 2015 (AHA) and 2015 (ESC)



From period 1 to period 3 they found a statistical significant increase in total number of IE recommendations from 37 to 253 ($p < 0.01$) (Managing treatments)

- There was a significant **decrease in LOE A**
- A non-significant **decrease in LOE B**
- A significant **increase in LOE C recommendations**

Consensus of opinion of the experts and / or small studies, retrospective, registries.

Conclusions:

- The number of IE guideline **recommendations has increased 6-7 fold** during the last decade without a corresponding increase in evidence.
- These results highlight the strong **need for multiple RCT** to improve the level of evidence.

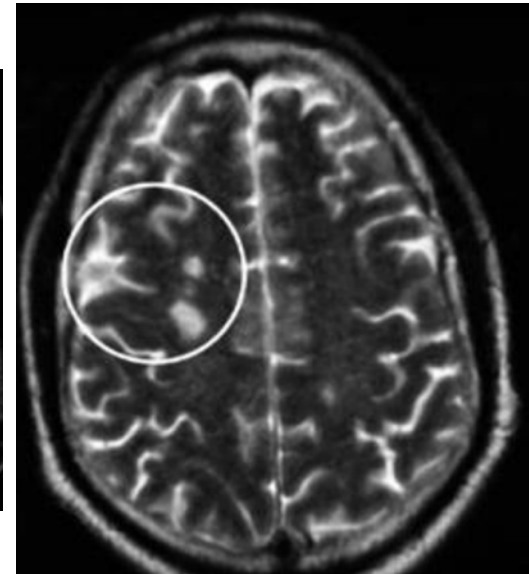
Main reasons of IE treatment

1. **Drug choice** due to pathogen and **bactericidal regiment** should be used
2. **Surgery** is used mainly **for treating structural cardiac complications, removing abscesses and sources of embolism**
3. Success relies on **eradication of pathogen**, clearing and debriding paravalvular infection, **removing of infected tissue, foreign material and hardware**



Other reasons for in H treatment in IE

- To treat associated infections
- To treat co-morbidities: dialysis, strokes, COPD, DM
- To reduce and treat frequent other complications:
 - Heart failure
 - Splenic abscess
 - Neurological
 - Acute renal failure
 - Conduction defects
 - Myocarditis
 - Pericarditis
 - Drug fever





Surgical Cure of *Candida albicans* Endocarditis with Open-Heart Surgery

Jerome Harold Kay, M.D.[†], Sol Bernstein, M.D.[‡], Donald Feinstein, M.D.[§], and Marjorie Biddle, Ph.D.[¶]

N Engl J Med 1961; 264:907-910 | May 4, 1961 | DOI: 10.1056/NEJM196105042641804

First to report surgical cure
with open-heart surgery
(TV vegetectomy) of pts with
medically resistant IE
(*Candida albicans*)



1965 - The first published case report of cardiac valve replacement for IE

They described a **45 year old** man with **Klebsiella endocarditis** affecting the aortic valve in whom severe aortic regurgitation and congestive heart failure developed which **failed to respond to medical therapy**. Excision of the valve and **replacement with a Starr-Edwards** prosthesis was **curative**.

The advent of a wide spectrum of bactericidal antibiotic agents has enabled physicians to treat many cases of bacterial endocarditis with a high likelihood of success. There remain, however, a significant number of patients with endocarditis in whom the infection is more resistant to antimicrobial therapy, valve destruction more rapid, and a satisfactory response to medical therapy sufficiently infrequent to warrant consideration of a new therapeutic approach.

Wallace A, et al. Treatment of Acute Bacterial Endocarditis by Valve Excision and Replacement. Circulation 1965;31:450-3



Article

June 5, 1967

Early Surgical Treatment of Valvular Endocarditis

Benson R. Wilcox, MD; Herbert J. Proctor, MD; Charles E. Rackley, MD; [et al](#)

› [Author Affiliations](#)

JAMA. 1967;200(10):820-823. doi:10.1001/jama.1967.03120230072008

Three patients with valvular destruction secondary to bacterial endocarditis were treated by early valvular re-
placement. Operative intervention prior to completion of the conventional prolonged course of antibiotic therapy
was necessitated by hemodynamic collapse in two patients and by drug resistance in a third patient. Six weeks
after valve replacement in the patient in case 1, he successfully underwent left pneumonectomy for carcinoma of
the lung. Following surgery, the three patients are doing well, with no evidence of infection or congestive heart
failure.

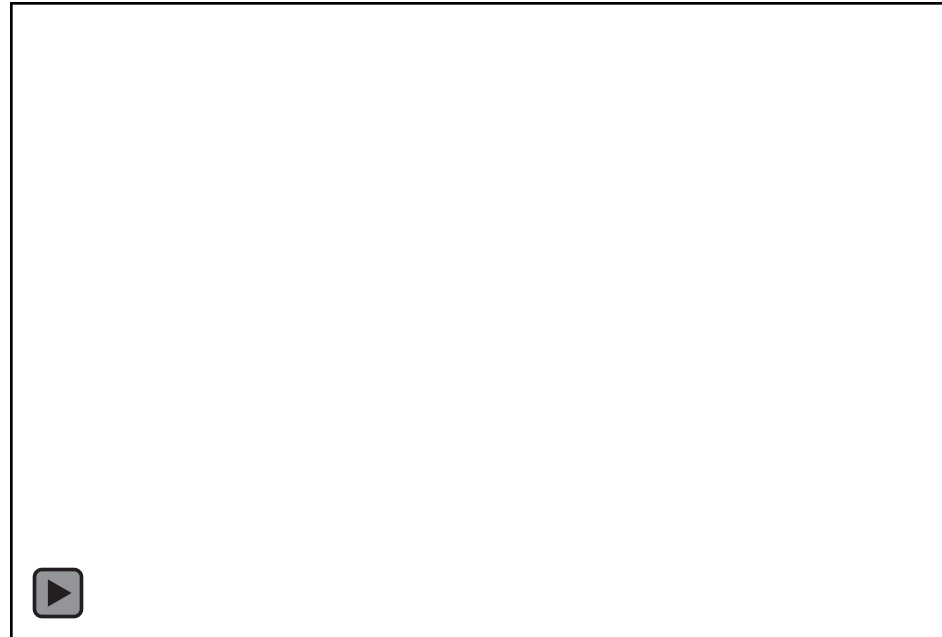
The dilemma as to “when” is the right time to perform surgery

- ❑ **Should we operate early** to reduce the risk of progressive deterioration of cardiac function?

or

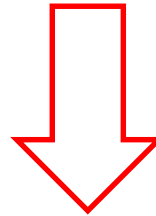
- ❑ **Should we perform the surgery after the effective control of infection** to reduce the surgical risks and complications?

This was the dogma!



A “paradigm shift” in the management of IE

- **Historically, the dogma was to avoid surgery during the acute phase,** since the tissues are inflamed and infected, making surgery very difficult, and leading to high postoperative mortality and high risk of valve dysfunction.



- **Over the past two decades, this dogma has changed dramatically,** owing the improvements in surgical techniques and earlier diagnosis. Although various surgical techniques have been used (e.g., mitral valve repair, aortic homograft implantation), a clear long-term **advantage of one technique has yet to be proven.** Regardless of approach, **the long-term results are inferior to elective valve surgery:** 10-year survival ranges from 40% to 60%

Infective endocarditis : Is it primarily a surgical disease ?

September 11, 2008 by dr s venkatesan

Infective endocarditis is a serious clinical cardiac problem. The disease has evolved over many decades and now we are witnessing the most virulent forms of the disease . Infection of heart , can occur in a native healthy valve, native diseased valve, or a prosthetic valve. Further, IE can occur either as an acute (usually non diseased valve) , or sub acute form (usually in diseased valve).The changing microbial pattern has made this entity very complex. The vigorous treatment protocols are available for IE. Still the prognosis and outcome with medical management is dismal even in best centers. So the role of surgery in IE has increased over the years.We propose here, a radically different approach to the problem.

Final remarks

- The 50% mortality in medical management is very high!
- Patients should be triaged early and the dominant theme should be surgery (cancer surgery): commonly valve replacement or valve repair.

ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

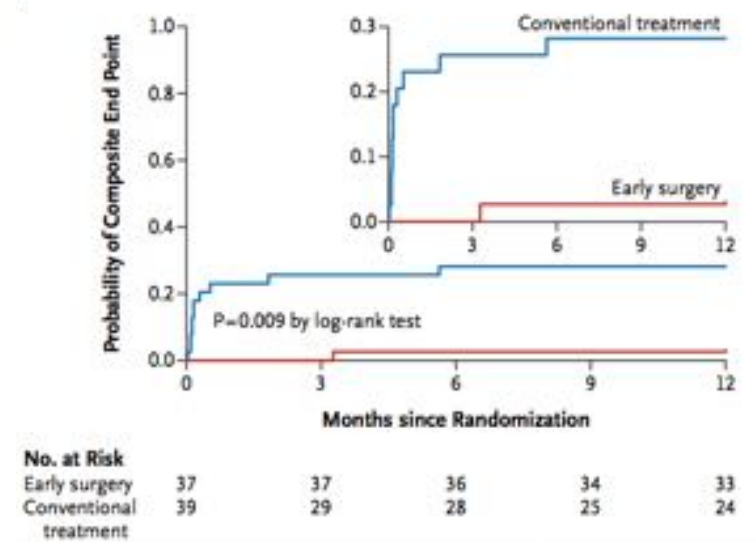
Duk-Hyun Kang, M.D., Ph.D., Yong-Jin Kim, M.D., Ph.D.,
 Sung-Han Kim, M.D., Ph.D., Byung Joo Sun, M.D., Dae-Hee Kim M.D., Ph.D.,
 Sung-Cheol Yun, Ph.D., Jong-Min Song, M.D., Ph.D.,
 Suk Jung Choo, M.D., Ph.D., Cheol-Hyun Chung, M.D., Ph.D.,
 Jae-Kwan Song, M.D., Ph.D., Jae-Won Lee, M.D., Ph.D.,
 and Dae-Won Sohn, M.D., Ph.D.

METHODS

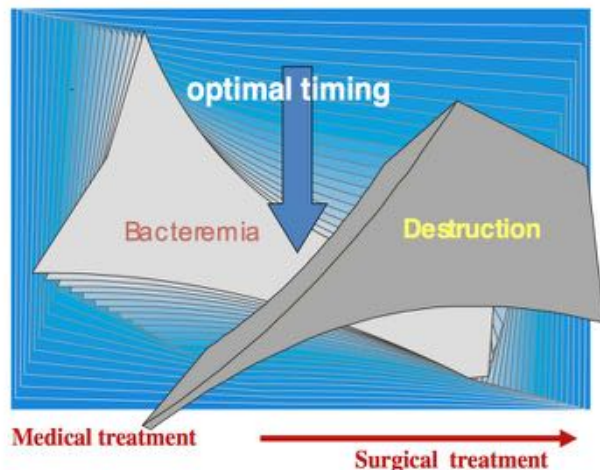
76 pts with left-sided IE (NO HF, abscess, fungal cause), severe valve disease and large vegetations (>10mm) randomized to early surgery (37 pts) or conventional treatment (27/39).

CONCLUSIONS

As compared with conventional treatment, early surgery in patients with infective endocarditis and large vegetations significantly reduced the composite end point of death from any cause and embolic events by effectively decreasing the risk of systemic embolism.

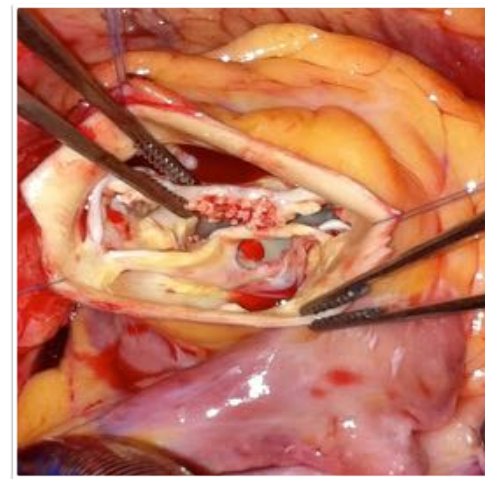


Timing of cardiac surgery in recent Guidelines



One major role of the “**endocarditis team**” is to define:

- **Optimal medical and antibiotic therapy**
- **The optimal timing of cardiac surgery**



The 2015 ESC guidelines provide an accurate staging of **early surgery, according to hemodynamic status**, that is graded as:

- “**emergency**” for surgery performed within 24 hours
- “**urgent**” for surgery performed in < 7 days (few days)
- “**elective**” when surgery is to be performed after at least 1-2 weeks of antibiotic therapy

The main indications for “early surgery” in AHA 2015 and ESC Guidelines 2015

	AHA Guidelines 2015 (8/9)	Class, Level of Evidence	ESC Guidelines 2015 (6/8)	Class, Level of Evidence	Timing†
Heart failure	Early surgery [‡] is indicated in patients with IE who present with valve dysfunction resulting in symptoms or signs of HF	I, B	Aortic or mitral NVE, or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary edema or cardiogenic shock	I, B	Emergency
	Early surgery [‡] is indicated in patients with PVE with symptoms or signs of HF resulting from valve dehiscence, intracardiac fistula, or severe prosthetic valve dysfunction	I, B	Aortic or mitral NVE, or PVE with severe regurgitation or obstruction causing symptoms of HF, or echocardiographic signs of poor hemodynamic tolerance	I, B	Urgent
Uncontrolled infection	Early surgery [‡] is indicated in patients when IE is complicated by heart block, annular or aortic abscess, or destructive penetrating lesions	I, B	Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	I, B	Urgent
	Early surgery [‡] is reasonable for patients with relapsing PVE	IIa, C			
	Early surgery [‡] should be considered, particularly in patients with IE caused by fungi or highly resistant organisms (e.g., VRE, multidrug-resistant gram-negative bacilli)	I, B	Infection caused by fungi or multiresistant organisms	I, C	Urgent/elective
	Early surgery [‡] is indicated for evidence of persistent infection (manifested by persistent bacteremia or fever lasting >5–7 d, and provided that other sites of infection and fever have been excluded) after the start of appropriate antimicrobial therapy	I, B	Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	IIa, B	Urgent
Prevention of embolism			PVE caused by staphylococci or non-HACEK gram-negative bacteria	IIa, C	Urgent/elective
	Early surgery [‡] is reasonable in patients who present with recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy	IIa, B	Aortic or mitral NVE, or PVE with persistent vegetations >10 mm after ≥1 embolic episode despite appropriate antibiotic therapy	I, B	Urgent
	Early surgery [‡] is reasonable in patients with severe valve regurgitation and mobile vegetations >10 mm	IIa, B	Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	IIa, B	Urgent
	Early surgery [‡] may be considered in patients with mobile vegetations >10 mm, particularly when involving the anterior leaflet of the mitral valve and associated with other relative indications for surgery	IIb, C	Aortic or mitral NVE, or PVE with isolated very large vegetations (>30 mm)	IIa, B	Urgent
			Aortic or mitral NVE, or PVE with isolated large vegetations (>15 mm) and no other indication for surgery	IIb, C	Urgent

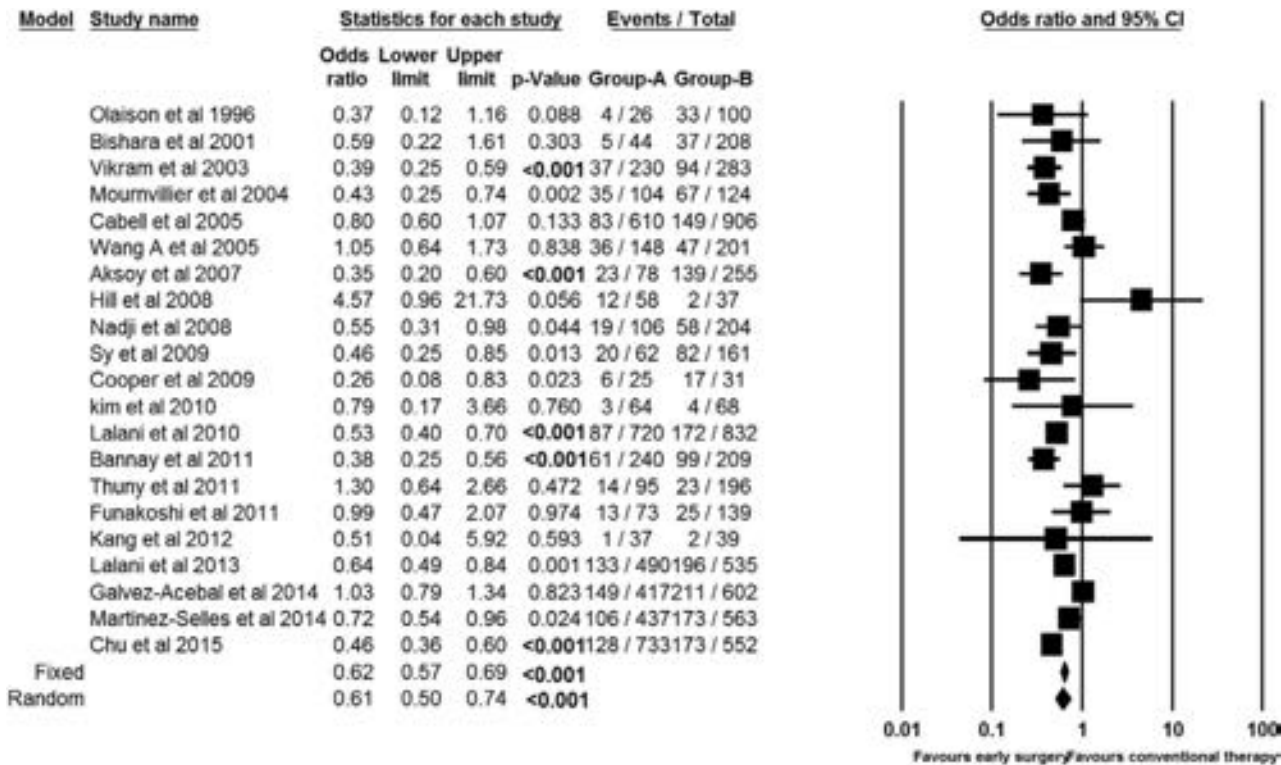
[‡]Defined as “during initial hospitalization and before completion of a full course of antibiotics.” †Defined as: emergency surgery – performed within 24 h; urgent surgery – within a few days; elective surgery – after at least 1 to 2 weeks of antibiotic therapy.

HACEK = *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Ellenella corrodens*, and *Kingella* species; HF = heart failure; NVE = native valve infective endocarditis; PVE = prosthetic valve infective endocarditis; VRE = vancomycin-resistant *Enterococcus*; other abbreviations as in Tables 1 and 2.

Early versus late surgical intervention or medical management for infective endocarditis: a systematic review and meta-analysis

Mahesh Anantha Narayanan,¹ Toufik Mahfood Haddad,¹ Andre C Kalil,²

21 studies



Conclusions: The results of our meta-analysis suggest that **early surgical** intervention is associated with **significantly lower risk of mortality** in IE

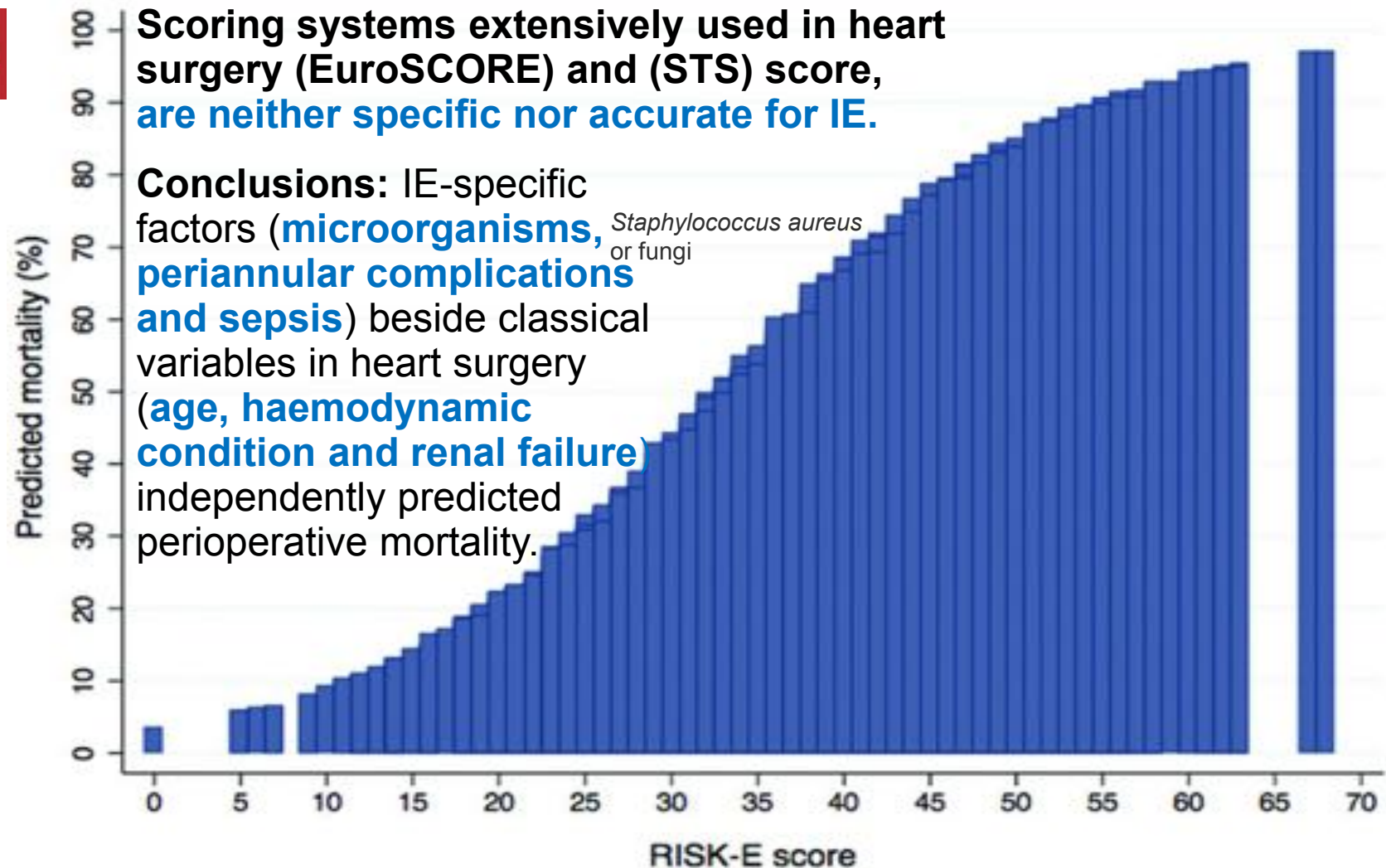


Risk stratification plays an important role in the decision-making for surgery in IE.

A prognostic scoring system, if accurate, could be of help in this scenario.

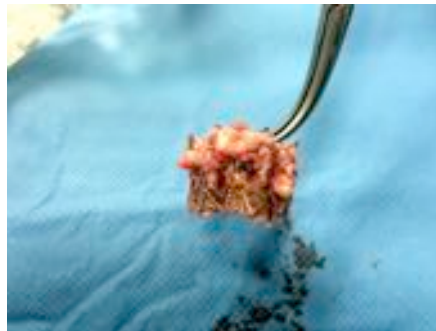
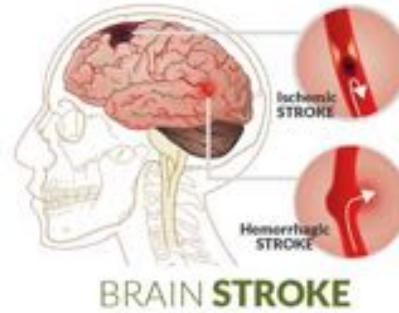
Predicted risk of postoperative mortality associated with individual RISK-E scores.

Heart



Contemporary management challenges in the treatments of IE

- **Stroke**
- **Cardiac Device Infection (CIEDs)**
- **TAVR**

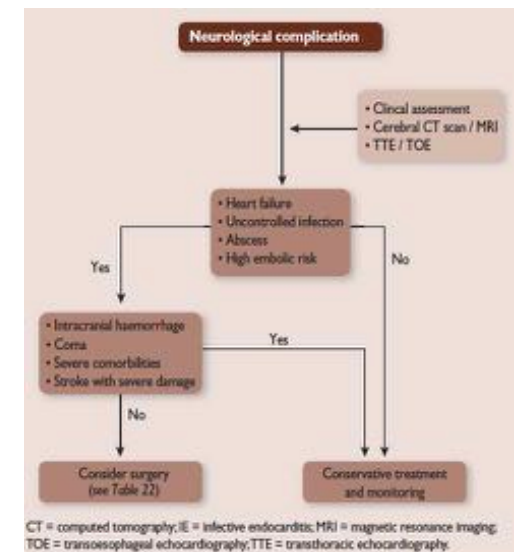


Neurological complications

- Symptomatic **neurological events develop in 15–30%** and are associated with **excess mortality**
- If cerebral haemorrhage has been excluded by cranial CT and **if neurological damage is not severe (i.e. coma), surgery should not be delayed in:**

- HF
- Uncontrolled infection
- Abscess
- Persistent high embolic risk

Can be performed with a low neurological risk (3–6%) and good probability of complete neurological recovery



- In cases with **intracranial haemorrhage neurological prognosis is worse** and surgery should generally be **postponed for at least 1 month**

Cardiac Device Infection

NCBI Resources How To

PubMed.gov

US National Library of Medicine
National Institutes of Health

PubMed



Cardiovascular Implantable Electronic Devices - CIEDs

Advanced

Format: Abstract +

Send to +

J Saudi Heart Assoc. 2016 Jul;28(3):167-9. doi: 10.1016/j.jsha.2015.12.007. Epub 2016 Jan 2.

An alien in the heart.

Agrawal Y¹, Kalavakunta JK², Gupta V².

⊕ Author information

Abstract

We report a case of a 38-year-old-man who presented with altered mental status. The patient was diagnosed with infective endocarditis (IE) originating from the GORE HELEX septal occluder device, which was placed 15 months earlier for symptomatic atrial septal defect. Brain imaging revealed shower emboli phenomena from the known IE. The patient developed hydrocephalus for which external ventriculostomy was performed. Improved neurological status warranted open heart surgery. The patient was later confirmed to be an intravenous drugs abuser prejudicing IE. This case highlights the importance of meticulously monitoring patients with suspected high-risk behavior with an implanted intracardiac prosthetic device.

KEYWORDS: Atrial septal defect; GORE HELEX septal occluder device; Infective endocarditis; Interatrial septum; Ventriculostomy

PMID: [27358534](#) PMCID: [PMC4917543](#) DOI: [10.1016/j.jsha.2015.12.007](#)



Andrea S Christopher

@andrea_sylvie

Segui



When treating infective endocarditis should involve treating opioid use disorders (hint hint: always)

Traduci dalla lingua originale: inglese



Stretching the Scope — Becoming Frontline Addiction-Med...

Perspective from The New England Journal of Medicine —
Stretching the Scope — Becoming Frontline Addiction-Medicine
Providers

nejm.org

14:40 - 25 ago 2017

2 Mi piace



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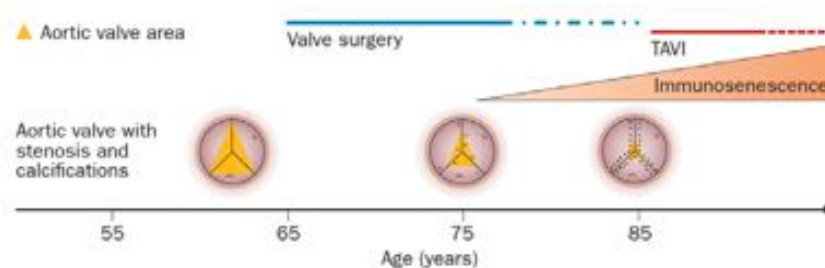


Twitta la tua risposta



El post-TAVI

- **L'El rappresenta un'inattesa condizione sfidante** anche perché abbiamo poche informazioni e raccomandazioni (0,5-3% ma nel Partner Trial a due anni 1,5% vs CCH 1%)
- **Il tasso di mortalità ospedaliera è del 36%**, a 2 anni del 67%
- **La diagnosi è più difficile** e probabilmente richiede tecniche multi-imaging da affiancare all'eco, come la CT o la PET/CT
- Il frequente **rigurgito paravalvolare aortico** dopo TAVI potrebbe giocare un ruolo determinante nel predisporre alla EI, così come uno **stato di immunosenescenza**



POET Study



Format: Abstract +

Am Heart J. 2013 Feb;165(2):116-22. doi: 10.1016/j.ahj.2012.11.006. Epub 2013 Jan 3.

Partial oral treatment of endocarditis.

Iversen K¹, Hest N, Bruun NE, Elming H, Pump B, Christensen JJ, Gill S, Rosenvinge F, Wiggers H, Fuursted Hassager C, Hefsten D, Larsen JH, Moser C, Ihlemann N, Bundgaard H.

⊕ Author information

Early hospital discharge is frequently facilitated by the use of outpatient parenteral antibiotic therapy (OPAT).

Abstract

BACKGROUND: Guidelines for the treatment of left-sided infective endocarditis (IE) recommend 4 to 6 weeks of intravenous antibiotics. Conversion from intravenous to oral antibiotics in clinically stabilized patients could reduce the side effects associated with intravenous treatment and shorten the length of hospital stay. Evidence supporting partial oral therapy as an alternative to the routinely recommended continued parenteral therapy is scarce, although observational data suggest that this strategy may be safe and effective.















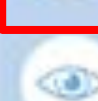
STUDY DESIGN: This is a noninferiority, multicenter, prospective, randomized, open-label study of partial oral treatment with antibiotics compared with full parenteral treatment in left-sided IE. Stable patients (n = 400) with streptococci, staphylococci, or enterococci infecting the mitral valve or the aortic valve will be included. After a minimum of 10 days of parenteral treatment, stable patients are randomized to oral therapy or unchanged parenteral therapy. Recommendations for oral treatment have been developed based on minimum inhibitory concentrations and pharmacokinetic calculations. Patients will be followed up for 6 months after completion of antibiotic therapy. The primary end point is a composition of all-cause mortality, unplanned cardiac surgery, embolic events, and relapse of positive blood cultures with the primary pathogen.

CONCLUSION: The Partial Oral Treatment of Endocarditis study tests the hypothesis that partial oral antibiotic treatment is as efficient and safe as parenteral therapy in left-sided IE. The trial is justified by a review of the literature, by pharmacokinetic calculations, and by our own experience.

TRIAL REGISTRATION: ClinicalTrials.gov [NCT01375257](https://clinicaltrials.gov/ct2/show/study/NCT01375257).

Conclusioni

- L'endocardite infettiva è ancora un vecchio problema clinico, con una veste nuova

I nostri sforzi		
Preventive strategies	Improving diagnosis	Optimal management
 Reduce hospital acquired bacteremia	 High index of clinical suspicion in at-risk groups	 Evaluation by an endocarditis team
 Good oral hygiene for at-risk groups	 Patient education	 Early risk stratification
 Antibiotic prophylaxis for high risk groups	 Early echocardiography	 Early transfer to center of expertise
 In future, antibacterial coatings/materials	 Adjunctive imaging if echocardiography non-diagnostic	 Tailored antibiotic therapy
	 Rapid microbiology results with antibacterial sensitivity	 Early surgery for selected patients No “cookbook” approach!
		 Monitoring for complications
<p>- E' ora di trasformare le sfide sul trattamento in risposte, magari con uno shift da studi osservazionali ai RCT</p>		<p>Looking for and treating the POE is important</p>